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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/782,184	02/12/2001	Howard Sands	12636-898	6040

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EXAMINER
GOLLAMUDI, SHARMILA S

ART UNIT	PAPER NUMBER
1616	8

DATE MAILED: 12/18/2001

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Applicati n No.

09/782,184

Applicant(s)

SANDS ET AL.

Examiner

Sharmila S. Gollamudi

Art Unit

1616

-- The MAILING DATE of this c mmunicati n appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM  
THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 12 February 2001 .
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-30 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-30 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.  
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All b) ☐ Some \* c) ☐ None of:  
1. ☐ Certified copies of the priority documents have been received.  
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).  
\* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).  
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_\_ .
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 6/7 .                      6) ☐ Other: \_\_\_\_\_ .

### **DETAILED ACTION**

Claims 1-30 are included in the prosecution of this application.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**Claims 1-30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

The independent claims are confusing. It is unclear from the claims whether the phospholipid layer surrounds each droplet or several droplets are enclosed within the phospholipid layer. Clarification is requested.

It is unclear from claim 19 whether the solid camptothecin recited in the second size distribution exists as such without the lipophilic liquid vehicle. The examiner suggests restructuring the claim for clarity.

What is being conveyed by "phospholipid comprises Lipoid 80" as recited in claim 23? Is it the applicant's intent to convey that phospholipid is Lipoid 80? The examiner suggests reciting the chemical name of Lipoid 80 in this claim and the other Lipoids recited in claim 22.

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

Application/Control Number: 09/782,184

Art Unit: 1616

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**Claims 1-8 and 12-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haynes (4725442) by itself or in combination with Burke (5552156).**

Haynes discloses microdroplets (200 angstroms up to a micron) of water insoluble drugs containing a pharmaceutically acceptable liquid surrounded by a layer of phospholipid (Note the abstract, columns 2-8, and claims). Haynes discloses the phospholipids that can be used (col. 5 and 6, line 56 to line 42).

Although Haynes discloses his invention using anesthetics in examples, according to the reference, the composition can be used to deliver any water insoluble/oil soluble drug via injection (col. 1, lines 26-39). Haynes further teaches anti-cancer agents as the drugs which can be practiced in his invention (note col. 8, lines 27-28).

Hayes does not specifically teach camptothecins as the anti-cancer drug.

Burke teaches the camptothecin drugs in lipid bilayers to overcome the insolubility and instability problems of camptothecin. Burke further discloses that the liposome creates an internal environment with a low pH to prevent hydrolysis of camptothecin drugs. (Note abstract) Further, Burke discloses that liposomes are routinely used to successfully administer cancer drugs to patients (col. 4, lines 47-48).

It is deemed obvious to one of ordinary skill in the art to use any hydrophobic drug including camptothecins, which are known in the art as anticancer drugs, with a

reasonable expectation of success since Haynes provides the general guidance to prepare the compositions.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to encapsulate camptothecins in Haynes's phospholipid layers in since Burke teaches the advantages of encapsulating camptothecins and liposomes successfully deliver cancer drugs.

**Claims 9-11 and 18-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Haynes (4725442) cited above or in combination with Burke cited above, further in view of WO 99/61001.**

As set forth above, Haynes discloses microdroplets (200 angstroms up to a micron) of water insoluble drugs containing a pharmaceutically acceptable liquid surrounded by a layer of phospholipid (Note the abstract, columns 2-8, and claims). Although Haynes discloses his invention using anesthetics in examples, according to the reference, the composition can be used to deliver any water insoluble/oil soluble drug via injection (col. 1, lines 26-39). Haynes further teaches that anticancer agents can be practiced in his invention (note col. 8, lines 27-28). As also pointed out above, Burke teaches claimed camptothecins encapsulated in lipid bilayer.

Haynes and Burke do not teach the inclusion of sugars such as mannitol or trehalose. The references also do not explicitly teach that the phospholipid-coated material can be sterilized.

WO 99/61001 discloses suspensions of submicron and micron sized particles of water insoluble biologically active substances containing lipoid and surface modifiers,

phospholipids. The reference also teaches that sugars such as trehalose and mannitol are thermoprotecting agents and should be included for protection during sterilization (note the abstract, Examples and claims). The reference also teaches the use of Lipoid E80 (Table 1).

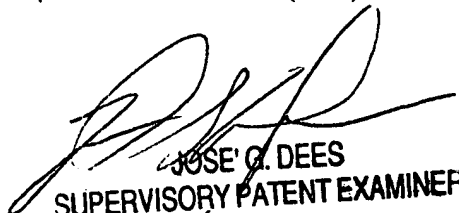
The inclusion of sugars such as trehalose or mannitol in the compositions of Haynes or Haynes and Burke would have been obvious to one of ordinary skill in the art at the time the invention was made since WO teaches that the instant sugars are thermoprotectants and protect the phospholipid particle suspensions during sterilization.

Any inquiry concerning this communication from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is (703) 305-2147. The examiner can be normally reached M-F from 7:30 am to 4:15pm.

If attempts to reach the examiner by the telephone are unsuccessful, the examiner's supervisor, Jose Dees, can be reached at (703) 308-4628. The fax number for this organization where this application or proceeding is assigned is (703) 308-4556.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist, whose telephone number is (703) 308-1235.

SSG

  
JOSE G. DEES  
SUPERVISORY PATENT EXAMINER  
1616